

Action in the order raised in that documents.

Prior Art.

The Examiner suggested that the applicant complete a Form PTO 1449 to comply with the rules on disclosure statements. Such a form is submitted herewith including the documents previously submitted to the Examiner by the applicant plus the additional ones submitted here.

In addition to the documents previously sent to the Examiner in conjunction with the filing of the preliminary amendment dated January 22, 1987, applicant wishes to bring to the attention of the Examiner three more documents. The first is a publication by Zhou et al., referred to on the Form 1449, which purports to demonstrate the Introduction of exogenous DNA into cotton embryos. This report of the alleged transformation of cotton relies on morphological changes to detect cotton transformation. The document contains no biochemical data from which one can verify that any transformation of any of the plants in question took place.

Copies of publications, subsequent to the filing date of this application, by Umbeck et al. and Firoozabady are enclosed, describing the genetic engineering of cotton plants. These documents are also referred in the PTO Form 1449.

Section 101 Rejection.

The Examiner has rejected Claims 14 and 16 to 21 under 35 USC Section 101 on the grounds that claimed invention is directed to non-statutory subject matter. The Examiner notes that the claims are drawn to plants and seed comprising cells containing DNA. The Examiner goes on to state, however, that it is unclear whether the DNA would impart a new trait or utility to the plant which would distinguish it from one occurring in nature.

While the applicant believes that the claims as filed distinguished over the cotton plants which could be found in nature, the applicant has amended Claims 14 and 17, from which all the Claims 14 and 16-21 depend, to specifically recite in each instance that the cotton plant includes cells which comprise in their genome

a gene which is foreign, recombinant and chimeric. These terms all indicate genetic material which is not found in any plant which occurs in nature. The defined genes inserted into the genome of these cells is thus foreign to the species, and consists of material from other organisms. In addition, the gene was created through recombinant techniques. These limitations make it clear that the gene itself is novel, at least in cotton, and does not occur in any naturally occurring cotton plant.

In addition, the claims specifically recite that the gene construction is effective in the cells of the plant to express a cellular product. While the claims are not limited to a particular cellular product, they are limited to genetic insertions which are effective to express products in the cells of the plant. Such cellular products can be detected, even if not phenotypically apparent, by appropriate biochemical assays. Thus, the language of the claims themselves makes it clear that a new trait, i.e., a genetic one, has been added to the plants as claimed in these claims which distinguish them from all plants which naturally occur.

In discussing the characteristics of a novel microorganism found patentable in Diamond v. Chakrabarty, 447 U.S. 303, 206 USPQ 193 at 197 (1980), the Supreme Court noted that an organism which was genetically modified was patentable if it was "a nonnaturally occurring manufacture or composition of matter," and later noted that the microorganism had "markedly different characteristics." The cotton plants claimed by the applicant are nonnaturally occurring in the sense that they have a genetic sequence which does not occur in any natural organism. The expression of those gene sequences in the cotton plants give them markedly and definably different characteristics from any cotton plants which have ever existed before, naturally or otherwise.

Accordingly, it is believed that the subject matter of the cotton seeds and plants claimed in Claims 14 and 16-21 are statutory subject matter within the terms of 35 USC Section 101.

Rejection under Section 112, second paragraph, to Claim 11.

In the Office Action the Examiner rejected Claim 11 under 35 USC Section 112 second paragraph as indefinite due to language informalities. Claim 11 has been amended herewith to specifically recite two separate Markush groups to make it clear which antibiotics may be present and which must be present. It is believed that this amendment to the language of this claim will obviate this rejection.

Deposit Rejection Under Section 112.

The Examiner has rejected the specification of this application and rejected all the claims thereof under 35 USC Section 112, first paragraph, on the grounds of failure to establish a proper deposit of microorganism.

Firstly, the applicant respectfully asserts that no deposit is required to enable the practice of the present invention, or to enable the practice of the best mode of the present invention. The present invention is directed toward the genetic engineering of cotton through Agrobacterium transformation, and to cotton plants which are transformed by the insertion of foreign genetic material. Vectors capable of expressing heterologous genes in plant cells are no longer novel and are widely available and used by many practitioners skilled in the art, although previously only with other species. Nothing about the method disclosed within the present application is dependent on the particular plasmid construction used by the applicants here, other than that the plant expression cassette used by the applicants has a selectable marker and includes an appropriate plant expression cassette. Similar selectable markers and plant expression cassettes are known and used by others of ordinary skill in the art. Therefore, the particular plasmids used by the applicant here to practice the invention are not necessary in order to practice the present invention, since equivalent plasmids are widely known and used in the art. Since the particular plasmids are not necessary to practice the invention, no deposit is required to enable this invention.

Nevertheless, to avoid misunderstanding, the applicant is submitting herewith a statement regarding deposit signed by the undersigned attorney to verify and state to the Patent Office that the deposited plasmid pCMC 1204 was deposited in accordance with the terms of the Budapest Treaty. In addition, the applicant has agreed to release all conditions on deposit upon the issuance of this patent application.

Therefore, while the applicant continues to assert that no deposit is necessary to enable the practice of the present invention, nevertheless the issue of deposit is obviated by the statement filed herewith and this rejection based on lack of enablement due to the deposit may be withdrawn.

Rejection of Claim 15 Under 102 (b) or 103

The Examiner has rejected Claim 15 of the present application under 35 USC 102(b) or 103 over the reference to Rangan et al. Rangan teaches the creation of somatic embryos in cotton tissues and culture. Therefore, argues the Examiner, Claim 15 of the present invention which is directed toward cotton somatic embryos produced by the method of Claim 2 is anticipated or obvious.

The applicant respectfully strongly disagrees with this assertion of either anticipation or obviousness based on the reference to Rangan. The cotton somatic embryos as claimed in Claim 15 are those which are produced by the method of Claim 2. The plain express language of Claim 2 specifically recites that the tissue which has been previously transformed by a culture of transforming Agrobacterium is cultured in the presence of a selection agent, which selects for plant cells transformed with the T-DNA transferred from the Agrobacterium, and further that the somatic embryos are induced in the tissue in that selection medium. Therefore, the express language of Claim 15, including the claims from which it depends, specifically recite limitations which make the somatic embryo of Claim 15 inherently different from those disclosed by Rangan. Most clearly the somatic embryos of Claim 15 expresses a resistance to a selection agent, which the somatic embryos of Rangan

do not. Further, the somatic embryos express this resistance to the selection agent because of the specific method of transformation, which is not in anyway suggested or made obvious by Rangan.

Therefore it is submitted that the subject matter of this claim is not either anticipated or suggested by this reference.

Rejection Under 102(b) or 103 over Adang

The Examiner has rejected Claims 14 and 16-21 under 102(b) or 103 in view of the reference to Adang. The reference to Adang et al. cited by the Examiner consists of an abstract from a European patent application number 142,924. Enclosed herewith are excerpts from the full text of that published European patent application. If the Examiner desires, the applicant will submit a complete copy. Only excerpts have been submitted here in view of the extreme length of that published application.

In the published application by Adang, in the specification on page 22 thereof, the application specifically recites that certain kinds of plants might theoretically be altered through the introduction of genes into them. The application then recites that in general certain plant families might be susceptible to genetic transformation, and among the families named is the family Malvacea, which includes cotton. The application published by Adang includes a table (Table 2) a copy of which is also enclosed, which lists a whole list of plants which are "recommended" for protection by the gene to which the application is directed.

In the actual examples of plant transformation contained in the Adang application, the only tissues which are actually reported as transformed are those of tobacco, sunflower and carrot. The specification of the application contains no teaching or explanation anywhere as to the introduction of foreign genes specifically into cotton. The only discussion directed toward cotton is that on page 22, enclosed herewith, which suggests that cotton is an "ideal choice" for the insertion of insecticidal protein gene.

It is asserted that Adang does not either teach or make obvious the genetic engineering of cotton. If anything, Adang suggests that

the genetic engineering of cotton is desirable, stating that cotton is an "ideal choice," without in anyway disclosing or suggesting how that genetic engineering may be done. Thus, contrary to the assertion of the Examiner, Adang et al. does not contain any "teaching of transformed cotton plants" but, instead, consists only of an idle speculation that perhaps transformed cotton plants might be achievable some day. Such idle speculation does not constitute an enabling disclosure sufficient to constitute prior art to the concept of the present invention.

Section 103 Rejection Over Conventional Cotton Plants and Seeds.

The Examiner's further rejected Claims 14 and 16-21 over conventional cotton plants and seeds known in the art at the time the claimed invention was made. The Examiner argues that the presense of additional DNA does not render the plants unobvious unless the DNA is sufficiently expressed to provide an unexpected characteristic.

The applicant respectfully assets that claims of the application as filed, including Claims 14 and 17, did specifically recite that the DNA in the plants was expressing. Note that Claim 14 was dependent from Claim 2, which specifically included a selection regime for the selection agent resistance gene which therefore had to express to survive the selection medium. Therefore any cotton plants produced by the method of Claim 2 would be expressing the selection agent resistance gene. This trait is clearly not one existing in native cotton plants, and is sufficiently expressed to provide the cotton tissue with an unexpected characteristic not present in prior non-transformed plants.

Nevertheless, to obviate any further difficulty with regard to this issue, Claims 14 and 17 have been amended to specifically recite, in even further detail, that the genomic foreign recombinant DNA produces a cellular product in the cells of the cotton plant. The cellular product is an unexpected characteristic produced by expression of the genetic material in the plant. In Claim 17 and new Claim 23 it has been specifically recited that the cellular

product is selected from the group consisting of a foreign protein and a negative strand RNA. Foreign proteins are clearly capable of providing an unexpected characteristic to the plant readily differentiated from prior plants. Negative strand DNAs are also capable of altering the phenotype of the plant by inhibiting the expression of endogeneous genes. Both foreign proteins and negative strand RNAs are detectable traits, since, at a minimum, biochemical analysis of the plants will reveal their presence. Thus the expression of the genetic material in the transformed cotton plants of Claims 14 and 16-21 have been clearly recited so as not to describe, and not to be obvious in view of, prior cotton plants which fail to have these characteristics.

Rejection Under 103 over Combination of References.

The Examiner has rejected all the claims in the application under Section 103 over references to DeBlock taken in view of references to Zutra and Rangan et al. The Examiner asserts that DeBlock teaches non-oncogenic Agrobacterium cultures, that Zutra teaches that cotton is a host for Agrobacterium and that Rangan teaches cotton somatic embryogenesis. The Examiner seeks to combine these references to assert that the method of Agrobacterium gene transfer taught by the applicant here is obvious.

The applicant asserts that this reasoning is incorrect. Genetic transformation of plants is a difficult procedure requiring two complimentary processes, as specifically discussed in the introduction to this patent application. These processes are transformation of tissues and regeneration of transformed tissues. In many plants it is possible to transform some tissues, and also to regenerate some tissues, but it is impossible today to regenerate any of the tissues which are transformable. For example, there are various kinds of haploid cultures of corn which are regenerable and the transformation of corn protoplasts is possible, but neither the transformation of regenerable haploid cultures or the regeneration of sexually mature corn plants from transformed protoplasts has been achieved in any reported instance. Similarly, many reports of the

regeneration of soybean tissues have been reported for many years, and various soybean tissues and genotypes are susceptible to Agrobacterium transformation, but only within the last month has the successful regeneration of genetically engineered soybean plant by Agrobacterium transformation been reported. Therefore it is asserted that the availability of transformation techniques from certain kinds of tissue cultures, and the fact that the species of plant is theoretically susceptible to Agrobacterium infection, does not make obvious the genetic engineering of a plant by Agrobacterium transformation. There is no guarantee that the appropriate tissues which can be transformed by Agrobacterium transformation are the same ones which may be suitably regenerated. Furthermore, selection is always unusually following Agrobacterium transformation, and selectable agents do not work in all plant species.

Furthermore, note that the method claims of the present application, and in particular Claims 1 and 22 specifically begin with the transformation, and later regeneration, of a specific tissue type, the hypocotyl tissue of immature cotton plants. The applicant specifically found that the hypocotyl tissue, when subjected to the transformation and regeneration regimen described in this patent application, prove particularly susceptible to transformation and regeneration to yield mature, sexually competent plants. The references cited by the Examiner, and in particular the reference to Rangan, do not describe how the hypocotyl tissue may be particularly utilized in such a process. Certainly there is no teaching anywhere that hypocotyl tissue may be transformed in a way that allows for a selection agent to be utilized to select for transformed tissues. Furthermore there is no teaching that after such a selection, the regenerative potential of the tissues remains so that fully mature and sexually competent plants can be obtained.

The state of the art of plant genetic engineering at the time of the filing of this patent application was one in which the genetic transformation of various models of plant species, such as tobacco, petunia and carrot, had become a well established fact of



technological development. At that time no major crop species had been successfully genetically transformed. Yet all these species have certain types of tissues which can be regenerated into whole plants and all the species have been demonstrated to be capable of genetic transformation at a protoplast level. Therefore, the applicant asserts that the creation of genetically engineered cotton plants, if obvious, would have been widely demonstrated by many individuals. To date, the only genetically engineered cotton plants which have been reported are those reported in the papers to Umbeck, by the inventors here) and the the paper by Firoozabady, et al. submitted also herewith. It is submitted by the applicant here that the underlying rationale for the 103 rejection of the Examiner here is a variant of "obvious to try" logic. While various parts of the processes utilized by the applicant had been demonstrated before, there was no indication anywhere in the art that those processes could be combined to successfully create transgenic cotton plants. It was the applicant here who demonstrated that this was possible. The method by which this had been accomplished is disclosed and claimed in this patent application, and it is not believed that the combination of prior references and a hindsight analysis makes that achievement obvious.

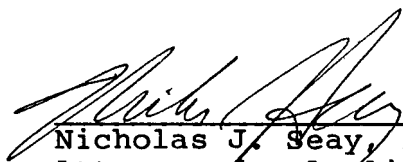
Drawing

A substitute formal drawing figure is enclosed herewith.

CONCLUSION

In view of the foregoing, reconsideration of the merits of this application is respectfully requested and an early and favorable reply solicited.

Respectfully submitted,



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